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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/833,782 | 04/12/2001 | D. Wade Walke | LEX-0161-USA | 1934 |

24231 7590 05/16/2003

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| EXAMINER |
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WALICKA, MALGORZATA A

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| ART UNIT | PAPER NUMBER |
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1652

DATE MAILED: 05/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/833,782

Applicant(s)

WALKE ET AL.

Examiner

Malgorzata A. Walicka

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02/29/03 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 02/29/03. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): of claim 5 under 35 USC section 112, 2nd.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 1-5.

Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☒ Other: Deadline search

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Amendment and Response to Final Office Action filed on April 29, 2003, as paper No. 15, is acknowledged.

The amendment to claim 5 has been added as requested. Claims 1-5 are pending in the application and are the subject of this Office Action.

Advisory Action

1. Rejections

1. 1. 35 USC section 112, second paragraph

Rejection of claim 5 made in the previous Office Action, paper No. 13, is withdrawn because the claim has been amended.

1. 2. 35 USC section 101

Claims 1-5 remain rejected under 35 U.S.C. 101 because the claimed invention lacks specific and substantial utility for the reasons set forth in the prior Office Actions, Paper No. 8 and 10 and 13.

In their response to the final rejection, paper No. 15, Applicants write,

"the Action [previous Office Action, paper No. 13, MW] disagrees with Applicants' logical assertion, based on the evidence, that the sequences of the present invention encode a novel human metalloprotease, specifically metallopeptidase M3, neurolysin. Applicants clearly assert this identity in the original specification. First in the

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title of the original application NOVEL HUMAN METALLOPROTEASE AND POLYNUCLEOTIDES ENCODING THE SAME. Second, second in the background information section of the specification, Section 2, Applicants describe the activity of metalloproteases including neurolysin. Thirdly, as emphasized in the instant Action (page 2) [previous Office Action, paper No. 13, MW], the Applicants identifies the structural similarities between mammalian neurolysin proteins and the sequence of the present invention" (page 2, line 17, of paper 15).

Applicants' argument has been fully considered but is found unpersuasive, because the specification does not provide Applicants' assertion that the claimed polypeptide is identified as neurolysin. However, Applicants argue that the assertion is given by:

- (a) the term "metalloprotease" comprised in the title,
- (b) the background section of the specification.

Applicants also suggest that the examiner herself emphasizes that Applicants identify the structural similarities between mammalian neurolysin proteins and the sequences of the present invention.

With respect to (a), the term "metalloprotease" is a generic term that covers thousands of enzymes, thus the term "metalloprotease" used alone cannot identify a

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particular metalloprotease. The term identifying the family, i.e., "metallopeptidase M3" quoted by the Applicants in their current response is absent from the specification.

With respect to (b), Applicants, page 1, line 10 of the specification, describe the novel protein as "a protein sharing sequence similarity with mammalian neurolysin proteins" without assertion of this very function for the protein encoded by the instantly claimed polynucleotides. Applicants do not even quote the percentage of homology of the novel protein to any mammalian neurolysin known at the time the application was filed. The phrase "sharing sequence similarity with mammalian neurolysin proteins" is not an assertion of function, but it refers to the structure of the claimed chemical compound. At the time application was filed the function of neurolysin was well established for mammals, so if Applicants were sure of the function of the claimed protein, they would have asserted it specifically.

The examiner emphasized in her last Office Action lack of the assertion of the function and not its presence. She wrote,

"the protein of SEQ ID NO: 2 encoded by DNA of SEQ ID NO: 1 was disclosed by Applicants as "a protein sharing sequence similarity with mammalian neurolysin proteins" (page 1, line 10), without quoting the percentage of homology to any mammalian neurolysin known at the time the application was filed. The phrase "sharing sequence similarity with mammalian neurolysin proteins" is not the statement of function, but it refers to the structure of the claimed chemical compound. At the time application was filed the function of neurolysin was well established for mammals, as Applicants proved by the

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content of the IDS. The characteristic features of neurolysin is that it cleaves neurotensin between residues Pro10 and Tyr11, and that it binds angiotensin. However, Applicants themselves did not present any evidence that protein of SEQ ID NO: 2 is able to cleavage neurotensin between residues Pro10 and Tyr11, and to bind angiotensin;" (the last Office Action, page 2, line 19 and further).

Thus, in summary, the assertion of the function of the new protein is missing from the specification.

Furthermore, in their response on page 3 line 29 Applicants argue,

"Additionally, the real world utility of the present invention is demonstrated by results obtained when a knockedout mouse was made in which the mouse gene encoding the ortholog of SEQ ID NOS: 1 and 2 of the present invention (human neurolysin (metalloproteinase M3 family) was disrupted by homologous recombination. These knockout mice were subject to a medical work-up using an integrated suite of medical diagnostic procedures designated to assess the function of the major organ system in a mammalian subject."

It is unclear whose results are the Applicants referring to in their response. Applicants themselves did not describe these results in the specification, neither as their

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own nor by quoting the other authors; thus Applicants' argument it is found not persuasive.

In addition to the arguments referred to above, Applicants reiterated their arguments presented in their previous responses, papers No 9 and 12.

The first argument is that the newly disclosed polynucleotides of SEQ ID NO: 1 can be used "on DNA chips" (page 4, line 14), which is a substantial, credible and specific utility. Applicants' argument is found not persuasive for the reasons presented in paper No. 10.

The second argument is that localizing the new gene on human chromosome is a specific utility (page 6, line 10). This argument is found not persuasive for the reasons stated in paper No. 10.

The third argument is that the Patent and Trade Mark Office itself [emphasis added by Applicants] has issued numerous patents on polynucleotides sequences that have not been directly shown to be associated with the function of the protein that is set forth in the specification. This argument has been found not persuasive for reasons presented in the Office Action No. 10.

1.3. Rejection under 35 USC section 112, first paragraph,

Claims 1-5 remain rejected under 35 USC section 112, first paragraph, because the claims are not supported by either a specific or substantial asserted utility for reasons indicated in Office Action No. 8, 10 and 13.

In their responses, papers No. 9 and 12, Applicants argue that utility of DNA molecule of SEQ ID NO: 1 is supported by the fact that it encodes SEQ ID NO: 2 that is identical to human neurolysin sequence disclosed by Chen et al., accession no. CAC27329, submitted to EMBL Jan 23, 2001, i.e., after 04/12/2000, which is the effective filing date for the instant application.

As indicated in the previous Office Action, paper No. 13, the fact that the third party scientists cloned the human neurolysin gene and disclosed the amino acid sequence of the enzyme after the Applicant filed the application does not change the fact that the protein of SEQ ID NO: 2 encoded by DNA of SEQ ID NO: 1 was disclosed by Applicants without asserting its function and utility. Applicants attention is also turned to the fact that even Chen et al. have, thus far, not disclosed actual enzymatic activity of the protein set forth by SEQ ID NO: 2 that is encoded by SEQ ID NO: 1, and which they call neurolysin. Search indicates that disclosure of the protein having the accession No. CAC27329 has not been followed by any publication by Chen or his co-workers. In addition, all what is currently known of human neurolysin is the DNA and amino acid sequence and characteristics based on homology to pig, rat, mouse and rabbit enzyme; see the attached.

In the current response, paper no. 15, Applicants state, on page 9, that Chen et al. likely have no knowledge of Applicants' efforts or the knockout mouse results described. It is unclear which results Applicants mean, and where they were described. The specification fails to present any results with knockout mice that could be and evidence of the invention's utility. Furthermore, the availability of post-filing date

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evidence of utility is irrelevant in the instant situation, where Applicants specification lacks any assertion of this utility. While post-filing evidence can be used to show that an assertion was correct, the assertion must have been present at the time of filing.

In summary, Applicants arguments and amendments have not placed the claims in conditions for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

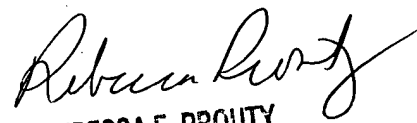
If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

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Patent Examiner


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